Decision Memo for Ventricular Assist Devices as Destination Therapy (CAG-00119N)

Decision Summary

CMS has determined that the evidence is adequate to conclude that implantation of a left ventricular assist device (LVAD) approved by the Food and Drug Administration (FDA) for destination therapy is reasonable and necessary as permanent mechanical cardiac support (destination therapy) for Medicare beneficiaries who have chronic end-stage heart failure (New York Heart Association Class IV end-stage left ventricular failure for at least 90 days with a life expectancy of less than two years), are not candidates for heart transplantation, and meet all of the following conditions:

1. The patient's Class IV heart failure symptoms have failed to respond to optimal medical management including dietary salt restriction, diuretics, digitalis, beta-blockers, and ACE inhibitors (if tolerated) for at least 60 of the last 90 days;
2. The patient has a left ventricular ejection fraction (LVEF) < 25%;
3. The patient has demonstrated functional limitation with a peak oxygen consumption of < 12 ml/kg/min; or the patient has a continued need for intravenous inotropic therapy owing to symptomatic hypotension, decreasing renal function, or worsening pulmonary congestion; and
4. The patient has the appropriate body size ($\geq$1.5 m^2) to support the LVAD implantation.

In addition, CMS has determined that LVAD implantation as destination therapy is reasonable and necessary only when the procedure is performed in a Medicare-approved heart transplant facility that, between January 1, 2001 and September 30, 2003, implanted at least 15 LVADs as a bridge to transplant or as destination therapy. These LVADs must have been approved by the FDA for destination therapy or as a bridge to transplant or have been implanted as part of an FDA investigational device exemption (IDE) trial for one of these two indications. LVADs implanted for support of blood circulation post cardiotomy or other investigational indications do not satisfy the volume requirement for this purpose. Since the relationship between volume and outcomes has not been well-established for LVAD use, facilities that have minimal deficiencies in meeting this standard may apply to the CMS Administrator for an exception based upon additional factors. Some of the factors we will consider are geographic location of the center, number of destination procedures done and patient outcomes from LVAD procedures completed.

Also, this facility must be an active, continuous member of a national, audited registry that requires submission of health data on all LVAD destination therapy patients from the date of implantation throughout the remainder of their lives. Such facility also must have in place staff and procedures that assure that prospective LVAD recipients receive all information necessary to assist them in giving an appropriate informed consent for the procedure so that they and their families are fully aware of the aftercare requirements and potential limitations as well as benefits following LVAD implantation.

CMS plans to develop accreditation standards for facilities that implant LVADs and, when implemented, LVAD implantation will be considered reasonable and necessary only at accredited facilities.

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Decision Memo

To: Administrative File: CAG 00119N
Ventricular Assist Devices as Destination Therapy

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Subject: Coverage Decision Memorandum for Ventricular Assist Devices as Destination Therapy

Date: October 1, 2003

I. Decision

CMS has determined that the evidence is adequate to conclude that implantation of a left ventricular assist device (LVAD) approved by the Food and Drug Administration (FDA) for destination therapy is reasonable and necessary as permanent mechanical cardiac support (destination therapy) for Medicare beneficiaries who have chronic end-stage heart failure (New York Heart Association Class IV end-stage left ventricular failure for at least 90 days with a life expectancy of less than two years), are not candidates for heart transplantation, and meet all of the following conditions:

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Also, this facility must be an active, continuous member of a national, audited registry that requires submission of health data on all LVAD destination therapy patients from the date of implantation throughout the remainder of their lives. Such facility also must have in place staff and procedures that assure that prospective LVAD recipients receive all information necessary to assist them in giving an appropriate informed consent for the procedure so that they and their families are fully aware of the aftercare requirements and potential limitations as well as benefits following LVAD implantation.

CMS plans to develop accreditation standards for facilities that implant LVADs and, when implemented, LVAD implantation will be considered reasonable and necessary only at accredited facilities.

II. Background

On August 9, 2002, CMS began a national coverage analysis for Ventricular Assist Devices as destination therapy for chronic, end-stage heart failure (ESHF). This action was taken in anticipation of a decision by the FDA on the then pending request to expand approval of the use of a left ventricular assist device for patients with ESHF who were not transplant candidates. The request for the coverage determination was initiated by four of the investigators who conducted the REMATCH study, the results of which had been published in The New England Journal of Medicine on November 15, 2001 and which provided most of the data that supported the FDA request.

Heart failure affects an estimated 5 million Americans, resulting in approximately 300,000 deaths annually. Heart failure is primarily a disease of the elderly. Eighty percent of those diagnosed with heart failure are over age 65 and 6-10 percent of the total Medicare population has this disease. As the leading cause of hospitalization in the Medicare population, heart failure accounts for 5-10 percent of total beneficiary hospitalizations.

Although patients with mild to moderate heart failure have been shown to benefit from drug therapy, the survival and quality of life for those with severe failure, whose symptoms fail to respond to optimum medical management, remains limited. Cardiac transplantation is the only treatment that provides substantial benefit for ESHF, but the available donor supply limits cardiac transplantation to approximately 3,500 patients worldwide per year. In 2000, there were 2,198 heart transplants performed in the United States. While eligibility criteria differ among transplant centers, most Medicare beneficiaries are excluded from receiving a heart transplant because of age or such comorbid conditions as diabetes with end organ damage, chronic renal failure or other chronic disease.

Ventricular assist devices are mechanical pumps that take over the function of the damaged heart (the right, left or both ventricles) and restore hemodynamics and end-organ blood flow. Different VAD designs, including electrically or pneumatically powered, either implanted or paracorporeal (external) currently have Food and Drug Administration (FDA) approval for the indications listed below. Most of these devices assist the left ventricle and, therefore, are commonly referred to as left ventricular assist devices (LVAD).

LVADs are currently used and approved for Medicare coverage in two groups of patients. The first group consists of patients who may require temporary ventricular support while recovering from cardiogenic shock following open heart surgery. The second group consists of patients who are not expected to recover adequate cardiac function, who have been approved for cardiac transplantation, and who require mechanical support to assist heart function until a donor heart becomes available. LVADs have been successfully used in this manner as a “bridge to transplant” for several years.

With bridge experience showing that LVADs could in some cases provide relatively long periods of cardiac support and considering the limitations of existing treatment options for ESHF patients, researchers investigated the use of LVADs as an alternative to transplantation for those patients who were not candidates for cardiac transplantation (“destination therapy”). Because the vast majority of these patients are over 65 years of age, this potential indication is of particular interest to the Medicare program.

III. History of Medicare Coverage

Currently, Medicare covers the implantation of an LVAD for patients with postcardiotomy complications and as a bridge to transplant in patients who have been approved as heart transplant candidates (Coverage Issues Manual section 65-15, Artificial Hearts and Related Devices):

A ventricular assist device (VAD) is used to assist a damaged or weakened heart in pumping blood. VADs are used as either a bridge to a heart transplant or for support of blood circulation postcardiotomy, which is the period following open heart surgery. VADs used for support of blood circulation postcardiotomy are covered only if they have received approval from the FDA for that purpose and the VADs are used according to the FDA approved labeling instructions. Since there is no authoritative evidence substantiating the safety and effectiveness of a VAD used as a replacement for the human heart, Medicare does not cover this device when used as an artificial heart.
All of the following criteria must be fulfilled in order for Medicare coverage to be provided for a VAD used as a bridge to transplant:
1. The VAD must be used in accordance with the FDA approved labeling instructions. This means that the VAD is used as a temporary mechanical circulatory support for approved transplant candidates as a bridge to cardiac transplantation;

2. The patient is approved and listed as a candidate for heart transplantation by a Medicare approved heart transplant center; and,
3. The VAD is implanted in a Medicare approved heart transplant center on a patient who is listed by that center. If the patient is listed by another Medicare approved transplant center, the implanting center must receive written permission from the center under which the patient is listed.
Centers implanting VADs should make every reasonable effort to transplant patients on such devices as soon as medically reasonable. Ideally, the centers should determine patient-specific timetables for transplantation and should not maintain such patients on VADs if suitable hearts become available.

Medicare does not presently cover this device as an alternative to medical management of ESHF patients who are ineligible for a heart transplant.

The Center for Medicare Management has determined that VADs as destination therapy fall within the Inpatient Hospital Services benefit category (section 1861 (b)(2) of the Social Security Act (the Act)), which describes supplies, appliances, and equipment furnished by the hospital, for use in the hospital, for the care and treatment of inpatients. After a VAD has been surgically implanted into the patient and when the patient is not a hospital patient, the replacement of an external part or parts may be covered under Medicare Part B within the Prosthetic Device benefit category (section 1861 (s)(8) of the Act).

IV. Timeline of Recent Activities

CMS received a request to expand Medicare coverage for use of these devices as destination therapy for ESHF patients who are not candidates for heart transplantation. The principal investigator of The Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH), Dr. Eric Rose, and three colleagues who were co-investigators, Dr. James W. Long, Dr. Leslie W. Miller and Dr. Lynne Warner Stevenson, submitted this coverage request.

August 9, 2002	CMS began a national coverage analysis for VADs as destination therapy.
August 12, 2002	Tracking sheet posted on CMS web site.
October 30, 2002	Decision made to refer issue to the Medicare Coverage Advisory Committee (MCAC).
March 12, 2003	MCAC panel meeting held.
May 21, 2003	MCAC meeting minutes and transcript posted on CMS web site.
June 11, 2003	Conference call held with the requestors to discuss registries.
September 5, 2003	Meeting with Thoratec and requestors to discuss payment issues.

V. FDA Status

On November 6, 2002, Thoratec, Inc. received FDA approval for an expanded Indication of Use for the Thoratec Heartmate SNAP VE LVAS for end-stage, non-transplantable patients. The approval states: “This device is now also indicated for use in patients with New York Heart Association Class IV end stage left ventricular failure who have received optimal medical therapy for at least 60 of the last 90 days, and who have a life expectancy of less than two years, and who are not eligible for cardiac transplantation. The device system is approved for use both inside and outside the hospital.”

CMS assesses relevant health outcomes, above and beyond the safety and effectiveness regulatory mandate of the FDA. Although a device must receive FDA approval or clearance for at least one indication to be eligible for Medicare coverage, FDA approval/clearance alone does not entitle that device to coverage. The device must fall under a Medicare benefit category and be determined to be reasonable and necessary for the diagnosis or treatment of an illness or injury or to improve the functioning of a malformed body member to be covered by CMS. CMS has the authority to conduct a separate assessment of a device’s appropriateness for Medicare coverage, including whether it is reasonable and necessary specifically for its intended use for Medicare beneficiaries (*see e.g.*, 60 FR 48417, 48420 (September 19, 1995). Under a premarket approval application (PMA) review, the FDA determines whether or not there is reasonable assurance of safety and effectiveness for the device’s intended use that is stated in its proposed labeling. Medicare NCDs consider the medical benefit and clinical utility of an item or service in determining whether the item or service is considered reasonable and necessary under the Medicare program. CMS determines whether or not the intervention improves net health outcomes in the Medicare population at least as well as established treatments. Thus, FDA PMA approval by itself is not sufficient for making a determination concerning Medicare coverage.

The same applies to FDA 510(k) clearance. As we stated in 66 FR 58788, 58797 (November 23, 2001), "[t]he criteria the FDA uses in making determinations related to substantial equivalency under section 510(k) of the Food, Drug, and Cosmetic Act is significantly different from the scientific evidence we consider in making "reasonable and necessary" determinations under Medicare. FDA does not necessarily require clinical data or outcomes studies in making a determination of substantial equivalency for the purpose of device approval under section 510(k) of the Food, Drug, and Cosmetic Act. Medicare NCDs consider medical benefit and clinical utility of an item or service in determining whether the item or service is considered reasonable and necessary under the Medicare program. Thus, a substantial equivalency approval under section 510(k) of FDA is not sufficient for making determination concerning Medicare coverage."

VI. General Methodological Principles

When making national coverage decisions, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding of reasonable and necessary. The evidence may consist of external technology assessments, internal review of published and unpublished studies, recommendations from the Medicare Coverage Advisory Committee, evidence-based guidelines, professional society position statements, expert opinion, and public comments.

The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) specific clinical questions relevant to the coverage request can be answered conclusively; and 2) the extent to which we are confident that the intervention will improve net health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the relevance of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's risks and benefits.

The issues presented here represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has unique methodological aspects.

1. Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to help ensure adequate numbers of patients are enrolled to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias)

- Co-interventions or provision of care apart from the intervention under evaluation (confounding)
- Differential assessment of outcome (detection bias)
- Occurrence and reporting of patients who do not complete the study (attrition bias)

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

- Randomized controlled trials
- Non-randomized controlled trials
- Prospective cohort studies
- Retrospective case control studies
- Cross-sectional studies
- Surveillance studies (e.g., using registries or surveys)
- Consecutive case series
- Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study's selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess the evidence.

2. Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage decisions for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation) and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations. The goal of our determination process is to assess net health outcomes, and we are interested in the results of changed patient management not just altered management. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

3. Assessing the Relative Magnitude of Risks and Benefits

An intervention is not reasonable and necessary if its risks outweigh its benefits. For all determinations, CMS evaluates whether reported benefits translate into improved net health outcomes. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

VII. Evidence

A. Introduction

1. CMS has reviewed articles, obtained input from the MCAC and reviewed numerous comments regarding expansion of current LVAD policy to include coverage of destination therapy. In addition, CMS met on a number of occasions with the principle investigators of the REMATCH trial, the only completed trial that has studied LVADs as destination therapy for which results have been published in peer-reviewed medical literature. A significant portion of background and trial information was provided through meetings with the requestors and investigators.

2. Outcomes of Interest

The most significant outcome of interest in evaluation of LVADs as destination therapy is all cause mortality. ESHF patients have a life expectancy of two years or less and medical management poorly controls the progression of disease. Having failed to qualify for a heart transplant, ESHF patients would benefit from any therapy that shows a clear advantage in mortality when compared to standard therapeutic options. An advantage in mortality as the result of this or any other therapy, however, must be weighed against the likelihood of adverse events or other negative consequences associated with its use, such as infection, prolonged hospitalization, or increased bleeding. However, all cause mortality is the appropriate outcome of interest.

In addition, patients undergoing LVAD implantation should experience an improved quality of life. A variety of instruments are available to measure both quality of life and functional status. Beyond mere extension of life, it is important that the patient be able to engage in the activities of daily living that offer satisfaction and make the extension of life worthwhile. Even if not able to return to all activities engaged in prior to illness, being able to live at home and freely leave it to visit family and friends would represent a significant improvement.

In addition to measurable outcomes for mortality and quality of life and functional status, the literature provides critical information on appropriate patient selection criteria for destination therapy. Due to the risks involved with implanting a LVAD it is important that the patient be fully apprised of those risks and carefully selected for the procedure. Additional consideration and review must also be given to the criteria for facilities to assure that patients have the best chance of increased life expectancy and improved quality of life following LVAD implantation. The devices are complicated and require a significant and long-term commitment of hospital resources to provide the necessary preoperative, surgical and postoperative care to maximize the patient’s chance at a successful outcome.

3. Instruments

Specific quality of life measures include the 36 Item Short Form (SF-36), the Minnesota Living With Heart Failure Questionnaire and the Beck Depression Inventory (BDI). The SF-36 scores quality of life based on the patient's perceived health status by using a multi-time scale to measure 8 health concepts: physical functioning, role physical, bodily pain, general health perceptions, vitality, social functioning, role emotional and mental health.[1] The Minnesota Living With Heart Failure Questionnaire is a 21-item survey that assesses the patients' perception of the effect congestive heart failure has on their lives.[2] Included are questions concerning physical, socioeconomic and psychological impairments. The BDI is a 21-item scale that measures symptoms or attitudes associated with depression.

Functional status in REMATCH was determined generally by the treating cardiologist or cardiac surgeon and consisted of reassessment of the NYHA classification. The New York Heart Association (NYHA) classification system is a physician's tool to identify the severity of heart failure based on patients' responses concerning their ability to perform ordinary physical activity.[3] The four classes are:

- Class I: Patients with no limitation of activities; no symptoms from ordinary activities.
- Class II: Patients with slight, mild limitation of activity; comfortable with rest or with mild exertion.
- Class III: Patients with marked limitation of activity; comfortable only at rest.
- Class IV: Patients who should be at complete rest, confined to bed or chair; any physical activity brings on discomfort and symptoms occur at rest.[4]

The assessment is a somewhat subjective evaluation based on patients' responses and the physician's knowledge of the patient.

Some patients were also quantitatively assessed with six minute hall walk and peak VO2 testing, but participation in such testing was low over all.

B. Discussion of evidence reviewed

1. Questions: CMS developed the following questions to assist in its review of the evidence:

a. Is the quality of the evidence adequate to draw conclusions about the net health outcomes in Medicare beneficiaries meeting the Randomized Evaluation of Mechanical Assistance for the Treatment of Heart Failure (REMATCH) trial criteria who undergo VAD implantation?

b. Do the results of the literature review indicate that CMS should require specific facility and personnel requirements that must be met to provide the patient with an optimal chance of successful VAD implantation?

c. Does the limited data available indicate that CMS should require ongoing data collection of all VAD implantation in Medicare beneficiaries to further refine appropriate patient selection and facility selection?

2. External technology assessments: None

3. Internal technology assessments

This review addresses the evidence related to the use of this device for destination therapy. The PubMed database was searched in February 2003 for peer-reviewed articles published from 1990 through January 2003. Search terms used included "heart-assist devices", "left ventricular assist devices", and "left ventricular assist systems" in any field and in conjunction with the terms “tranplant*” and “heart disease/failure” in the abstract. This search yielded 157 references. Abstracts were reviewed for studies, which specifically evaluated the use of this device in patients with ESHF who were not eligible for transplantation and received an LVAD specifically as destination therapy. Several articles included reports on patients who had received LVADs in anticipation of transplantation and then either recovered cardiac function (obviating the need for a transplant) or who for various other reasons did not receive a new heart thus becoming long-term LVAD patients. However, the only articles that met our inclusion criteria related to the REMATCH study and specifically dealt with the use of LVADs for destination therapy.

CMS staff also included several articles that contained relevant background and/or other pertinent information to this coverage review. In addition, CMS received citations from both the requestors and other interested parties. As a result, we have included several additional articles for review that provide information relevant to this topic. In addition, the ACC/AHA 2001 document “Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult” was included, as was a Consensus Conference report related to mechanical circulatory support, “Mechanical Cardiac Support 2000: Current Applications and Future Trial Design.”

Selected articles are summarized in the attached evidence table.

The REMATCH Trial: Rationale, Design, and End Points. Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure – 1999

The rationale for conducting REMATCH, obstacles to designing randomized surgical trials, lessons learned in conducting a multi-center pilot study and features of the REMATCH study design (objectives, target population, treatments, end points, analysis, and trial organization) are presented by the principal investigators.

The authors describe the unique challenges in conducting this randomized surgical clinical trial including the skill of the surgeon and the support available at a particular site. They also discuss the potential impact of refinement of the procedure during the trial, ethical issues related to random assignment, and the impossibility of blinding of the treating surgeon.

The purpose of REMATCH was to “evaluate the efficacy, safety, and cost-effectiveness of “wearable” LVADs versus optimal medical therapy in the treatment of end-stage heart failure”. The randomized controlled study’s primary purpose was to determine the effect of the LVAD on mortality from all causes with a broad range of secondary objectives, including use of hospitalization, functional status and quality of life.

The three main objectives were to obtain data on patient and device survival and to plan for a large-scale clinical trial of LVAD use in an older and sicker population than had previously received the device, to familiarize the surgeons with device modifications, and to meet an FDA mandate to determine whether randomization was feasible in a surgical trial for a life-threatening condition.

The study population included adult NYHA class IV patients who were ineligible for cardiac transplantation because of age greater than 65 or any of the following conditions: insulin-dependent diabetes with end organ damage; chronic renal failure with creatinine greater than 2.5 ml/dL for longer than 90 days; or any major comorbidity (physical or psychiatric) that would make them ineligible for transplantation. Additionally, the patient must have been on a regimen of digoxin, diuretics, and an angiotensin-converting enzyme (ACE) inhibitor (unless intolerant) for at least 90 of the 120 days prior to randomization

The trial was a parallel group study with random assignment of eligible patients to implantation of an LVAD or optimal medical management in a 1:1 ratio. The hypothesis was that the LVAD would reduce by a third the 2-year mortality in ESHF patients from 75% to 50% or more. To detect a difference of this magnitude with 80% power it was determined that 92 deaths would need to occur.

The investigators expected to gain information about the long-term effect of LVADs on survival, quality of life, and costs, which were considered critical in determining the role of this treatment option in end-stage heart failure. Both public and private support was obtained for this multisite study, which began enrolling patients in May 1998.

The Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) – 2001

Design: This randomized clinical trial was conducted at experienced cardiac transplantation centers under cooperative agreement between Columbia University, NIH and the manufacturer of the study device, Thoratec. Patients were randomly assigned (1:1) to either vented electric LVAD or optimal medical therapy. An independent morbidity and mortality committee reviewed causes of death and adverse events. The trial was designed to enroll 140 patients and to continue until 92 deaths had occurred.

Sample Size: 129 patients were enrolled and randomized with 68 in the LVAD group and 61 in the optimal medical management. The trial terminated at the 92nd death.

Primary endpoint: Death from any cause

Secondary endpoints: Incidence of serious adverse events (caused death or permanent disability, were life-threatening, or required or prolonged hospitalization), number of days of hospitalization, quality of life, symptoms of depression, and functional status.

Inclusion Criteria:
Adults with chronic end-stage heart failure and contraindications to transplantation:

- Symptoms of NYHA class IV heart failure for $\geq$ 90 days despite ACE inhibitors, diuretics and digoxin;
- LVEF $\leq$ 25%;
- Peak O_2 consumption $\leq$ 12 ml/kg or continued need for IV inotropic therapy for symptomatic hypotension, decreasing renal function or worsening pulmonary congestion;
- Patients could continue to receive beta-blockers if administered $\geq$ 60 of 90 days before randomization.

18 months after the start of the trial, the entry criteria was expanded in order to increase enrollment:

- NYHA class IV heart failure for ≥ 60 days;
- Peak O_2 consumption ≤ 14 ml/kg;
- Patients in NYHA class III/IV for ≥ 28 days, received ≥ 14 days support with intra-aortic balloon pump or dependent on IV inotropic agents, with 2 failed weaning attempts.

Three (3) LVAD patients and two (2) medical therapy patients enrolled under the expanded criteria.

Transplantation was contraindicated for at least one of the following reasons:

- Age > 65 years;
- Insulin-dependent diabetes mellitus with end-organ damage;
- Chronic renal failure (serum creatinine > 2.5.mg/dl for ≥ 90 days before randomization);
- Presence of other clinically significant conditions.

Exclusion Criteria

Cause of heart failure due to or associated with uncorrected thyroid disease, obstructive cardiomyopathy, pericardial disease, amyloidosis, or active myocarditis;

Technical obstacles that pose an inordinately high surgical risk in the judgment of the certified surgeon;

International normalized ratio > 1.3 or prothrombin time > 15 seconds within 24 hours before randomization;

Body surface area < 1.5 m^2;

Body mass index > 40 kg/m^2;

Severe chronic obstructive pulmonary disease as evidenced by forced expiratory volume ≤1.5 L/min;

If premenopausal, positive serum pregnancy test;

Fixed pulmonary hypertension with pulmonary vascular resistance ≥ 8 Wood units that is unresponsive to pharmacological intervention, documented within 90 days before randomization;

Patient under consideration for conventional revascularization procedure, therapeutic valvular repair, left ventricular reduction procedure (i.e., Battista), or cardiomyoplasty;

History of cardiac transplantation, left ventricular reduction procedure, or cardiomyoplasty;

Presence of implanted mechanical aortic valve that will not be converted to bioprosthesis at time of LVAD implantation;

Evidence of intrinsic hepatic disease defined as liver enzyme values (aspartate aminotransferase, alanine aminotransferase, or total bilirubin) > five times the upper limit of normal within 4 days before randomization or biopsy-proved liver cirrhosis;

Occurrence of stroke within 90 days before randomization or history of cerebrovascular disease with major (> 80%) extracranial or carotid stenosis documented by Doppler study;

Confirmation by neurologist of impairment of cognitive function, presence of Alzheimer's disease or any other form of irreversible dementia, or both;

Evidence of untreated abdominal aortic aneurysm $\geq$ 5 cm as measured by abdominal ultrasound within 30 days before randomization;

Suspected or active systemic infection 48 hours before randomization;

Platelet count 50 X 10/mm^3 within 24 hours before randomization;

Serum creatinine $\geq$ 3.5 mg/dL or regimen of long-term dialysis;

Major peripheral vascular disease accompanied by pain on rest or leg ulceration;

Receiving calcium-channel blocker (except amlodipine besylate) or type I (e.g., quinidine, procainamide hydrochloride, disopyramide phosphate) or type III antiarrhythmic agent (e.g., encainide hydrochloride, flecainide acetate, propafenone hydrochloride, moricizine hydrochloride) within 28 days before randomization;

Abdominal operation planned;

Recent history of psychiatric disease (including drug or alcohol abuse) that is likely to impair compliance with study protocol;

Receiving therapy with investigational intervention or participating in another clinical study;

Presence of condition other than heart failure that would limit survival to less than 3 years;

Enrollment: Block randomization was used to ensure equivalence of group size and was stratified according to center. The eligibility of patients was determined by investigators at each site and confirmed by a gatekeeper at the coordinating center. Optimal medical management patients (OMM) followed guidelines developed by the medical committee, with the goals of optimizing organ perfusion and minimizing symptoms of CHF. Their medications included digoxin, diuretics, ACE inhibitors and beta-blockers as directed by heart failure specialists.

Results:

Mortality: Kaplan-Meier survival analysis showed a reduction of 48 percent in the risk of death from any cause in the group that received left ventricular assist devices as compared with the medical therapy group (relative risk, 0.52; 95 percent confidence interval, 0.34 to 0.78; P=0.001). The rates of survival at one year were 52 percent in the device group and 25 percent in the medical-therapy group (P=0.002) and the rates at two years were 23 percent and eight percent (P=0.09), respectively. The rate of survival of device patients on an intent-to-treat basis at one year following surgery was 51 percent compared to 28 percent for the medical management patients. At two years, 29 percent of device patients survived as compared to 13 percent of the medical management group (data for both periods updated through January 15, 2003). By the time of the updated report three (3) medical management patients had crossed over to become LVAD recipients. Without the crossovers medical management survivorship was eight percent.

REMATCH was designed to enroll 140 patients and to continue until 92 deaths had occurred. These figures were based on the assumptions that there would be a two-year mortality in the medical management group of 75%, that implantation of the device would reduce mortality by 33 percent, and that the study would have a 90 percent power to detect a significant difference in mortality between the two groups. By the time the 92nd death occurred, 129 patients had been enrolled. Ultimately, the mortality rate for both groups in the study was higher than predicted and was likely due to the severity of illness in study participants. Overwhelmingly, the cause of death for medical management patients was left ventricular dysfunction, while device patients died from such device related causes as sepsis and device malfunction.

Quality of Life: Secondary endpoints evaluated in REMATCH included improved quality of life and functional capacity. Data reported at one year for study participants (both in the published study and in post publication data later reported to the FDA and CMS) showed an advantage for device recipients. While nearly all of the LVAD patients were assessed with these instruments, only about half of the medical management group was assessed. At one year the reported median NYHA class for device recipients had improved to class II, while the median class for medical management patients remained class IV. Objective functional status measures such as 6 minute hall walk distance and peak oxygen consumption were not available for comparison purposes.

Adverse Events: The frequency of serious adverse events in the device group was 2.35 (95 percent confidence interval, 1.86 to 2.95) times that in the medical-therapy group, with a predominance of infection, bleeding, and malfunction of the device. Surgery and treatment of complications meant that LVAD recipients experienced a higher number of days of hospitalization than did the medical management group, but because of the longer lifespan of surviving LVAD patients, they spent over three times as many days out of the hospital.

Author's Conclusions: "The use of a left ventricular assist device in patients with advanced heart failure resulted in a clinically meaningful survival benefit and an improved quality of life. A left ventricular assist device is an acceptable alternative therapy in selected patients who are not candidates for cardiac transplantation."

Mechanical Circulatory Support for Advanced Heart Failure: Effect of Patient Selection on Outcome – 2001

Methods: Data were obtained from the Novacor European Registry. Between 1993 and 1999, 464 patients were implanted with the Novacor LVAS in 22 European centers, of which 11 centers have performed > 10 implants each. Multivariate regression analysis was conducted to identify factors for survival after Left Ventricular Assist System (LVAS) implantation.

Because this model (N100 PC) was released in Europe as a commercial product, clinicians in participating centers were not bound by the constraints of an investigational protocol and predefined implantation criteria. This resulted in patient selection practices that varied greatly between centers. In addition, a large percentage of patients were moribund at the time of implantation. Examination of the consequences of this less rigorous patient selection is one of the major purposes of the study. The Novacor Registry began in 1997 at the instigation of a number of clinicians (European Advisory Board) who were active in the use of mechanical circulatory support (MCS) in an endeavor to promote an evidence-based perspective in mechanically supported advanced heart failure patients. The format for data collection and definitions of complications were a result of an expert consensus process and the system was refined over subsequent years.

Results: The majority of patients had idiopathic (60%) or ischemic (27%) cardiomyopathy. The median age at implant was 49 years (range 16 to 75). The median support time was 100 days (4.1 years maximum). Forty-nine percent of the recipients were discharged from the hospital on LVAS. These patients spent 75% of their time out of the hospital. For a subset of 366 recipients for whom a complete set of data was available, multivariate analysis revealed that the following preimplant conditions were independent risk factors for survival after LVAS implantation: respiratory failure associated with septicemia (odds ratio 11.2), right heart failure (odds ratio 3.2), age >65 years (odds ratio 3.01), acute postcardiotomy (odds ratio 1.8), and acute infarction (odds ratio 1.7). For patients without any of these factors, the 1-year survival after LVAS implantation including the posttransplantation period was 60%; for the combined group with at least 1 risk factor, it was 24%.

Authors' Conclusions: Careful selection, implantation while patients can still derive benefit, and improvement in management may result in improved outcomes of LVAS treatment for advanced heart failure.

Multicenter Clinical Evaluation of the HeartMate Vented Electric Left Ventricular Assist System in Patients Awaiting Heart Transplantation – 2001

Background: Despite advances in heart transplantation and mechanical circulatory support, mortality among transplant candidates remains high. Better ways are needed to ensure the survival of transplant candidates both inside and outside the hospital.

Methods: Prospective, (non-randomized) multicenter clinical trial conducted at 24 centers in the United States. Study population included 280 transplant candidates (232 men, 48 women; median age, 55 years; range, 11-72 years) unresponsive to inotropic drugs, intra-aortic balloon counterpulsation, or both, who were treated with the HeartMate Vented Electric Left Ventricular Assist System (VE LVAS). A cohort of 48 patients (40 men, 8 women; median age, 50 years; range, 21-67 years) not supported with an LVAS served as a historical control group. Outcomes were measured in terms of laboratory data (hemodynamic, hematological, and biochemical), adverse events, New York Heart Association functional class and survival.

Results: The VE LVAS-treated and non-VE LVAS-treated (control) groups were similar in terms of age, sex, and distribution of patients by diagnosis (ischemic cardiomyopathy, idiopathic cardiomyopathy, and subacute myocardial infarction). VE LVAS support lasted an average of 112 days (range, < 1-691 days), with 54 patients supported for > 180 days. Mean VE LVAS flow (expressed as pump index) throughout support was 2.8 L/min/m^2. Median total bilirubin values decreased from 1.2 mg/dL at baseline to 0.7 mg/dL ($p = 0.0001$); median creatinine values decreased from 1.5 mg/dL at baseline to 1.1 mg/dL ($p = 0.0001$). VE LVAS-related adverse events included bleeding in 31 patients (11%), infection in 113 (40%), neurologic dysfunction in 14 (5%), and thromboembolic events in 17 (6%). A total of 160 (58%) patients were enrolled in a hospital release program. Twenty-nine percent of the VE LVAS-treated patients (82/280) died before receiving a transplant, compared with 67% of controls (32/48, $p < 0.001$). Additionally, 71% of the VE LVAS-treated patients (198/280) survived; 67% (188/280) ultimately received a heart transplant and 4% (10/280) had the device removed electively. One-year post-transplant survival of VE LVAS-treated patients was significantly better than that of the comparison group (84% patients were alive vs 63% $p = 0.0197$).

Authors' conclusions: The HeartMate VE LVAS provides adequate hemodynamic support, has an acceptably low incidence of adverse effects, and improves survival in heart transplant candidates both inside and outside the hospital. The studies of the HeartMate LVAS (both pneumatic and electric) for Food and Drug Administration approval are the only studies with a valid control group to show a survival benefit for cardiac transplantation.

Performance of the LVAD outside of the hospital was one of the key points of this study and patients receiving the device consented to release from the hospital following implantation, if qualified. Qualifications included achieving a NYHA class of I or II. 115 of 228 potentially eligible patients achieved full outpatient status while using an LVAD as a bridge to transplant. Forty-five additional patients were able to leave the hospital for day trips, but were not fully released. For the cohort of fully and partially released patients (n=160), 138 ultimately received a transplant, ten elected to have the LVAD removed without transplant and twelve died while awaiting transplant. Five of the explanted patients achieved myocardial recovery; four were explanted due to infection and one due to pump malfunction.

4. MCAC

The Medicare Coverage Advisory Committee Meeting met March 12, 2003 to review the evidence relating to the use of LVADs as destination therapy in the Medicare population and to discuss related issues (http://www.cms.gov/mcd/viewmcac.asp?id=79). Two voting questions were posed to the panel:

- Is the quality of the evidence adequate to draw conclusions about the net health outcomes in Medicare beneficiaries meeting the Randomized Evaluation of Mechanical Assistance for the Treatment of Heart Failure (REMATCH) trial criteria who undergo LVAD implantation?

- If the quality of the evidence is adequate, does it demonstrate any positive net health outcomes and if so what is the size of the net health outcomes of LVADs compared to optimal medical management for these patients?

The principal REMATCH investigators presented the results of their study, including updated data, and answered questions from the committee. After a thorough discussion of the study, the committee voted six to one in the affirmative on the first question. After further discussion, five panel members voted on question two that the size of the net health effect was "substantially more effective", while two considered it "more effective".

Panelists were also asked to discuss, but not vote on additional questions relating to the need for mandatory reporting of health data as a condition for Medicare reimbursement, the need for specific facility and personnel requirements to provide destination therapy, methodology for determining that a patient was not a cardiac transplant candidate and whether the increased risk of adverse events associated with implantation of an LVAD was adequately offset by the demonstrated extension of life and improvement in its quality. There was strong support for limiting facilities to those with demonstrated excellence in the procedure and to requiring a national registry.

5. Evidence-based guidelines

CMS was unable to locate any guidelines for the implantation of LVADs for destination therapy.

6. Professional Society Position Statements

Consensus Conference Report: Mechanical Cardiac Support 2000: Current Applications and Future Trial Design: June 15–16, 2000 Bethesda, Maryland – 2001

This conference was held to assess current mechanical support applications and future trial designs for investigation of heart failure. The report outlines uses and limitations of cardiac support devices available at the time of writing. They point out that "(o)f the more than 3,000 patients who have been implanted with circulatory support devices as a bridge to transplantation, approximately 60% to 70% actually received a transplant. Of those that received a transplant, 85% to 90% survived to be discharged from the hospital. Among those implanted as a bridge to transplantation, approximately 5% recovered ventricular function and survived without transplantation… During the past year, at least 50% of patients receiving wearable LVADs have been able to be discharged from the hospital, and patients have been supported from periods of a few weeks to >4 years." Upon completion of successful studies proving the utility of LVADs for "destination therapy", those devices could be considered as an alternative to transplantation for "the 50,000 to 100,000 patients in the U.S., who have been estimated to potentially benefit from this technology."

7. Expert Opinion

The American College of Cardiology (ACC) submitted a letter in support of expanded coverage of LVADs to include destination therapy. The ACC commented that detailed inclusion and exclusion criteria along with criteria for facilities, "…should allow only those selected patients with truly refractory heart failure to undergo this procedure and limit overzealous application." In addition the ACC commented that current reimbursement for LVADs is inadequate and should be adjusted to reflect reasonable cost. The American Society of Transplant Surgeons also submitted a letter in support of expanding coverage for LVADs to include destination therapy.

CMS received opinions from experts concerning the mandatory use of a registry for patients undergoing VAD implantation as destination therapy. Experts at the Heart Failure Society of America recommended that, “Such a database will enable ongoing refinement of patient selection criteria and institutional eligibility, as well as enable continuous quality improvement in the use of this emerging therapy.”[5] In addition to overall support of a registry, the American College of Cardiology, American Heart Association, Society of Thoracic Surgeons, American Society for Artificial Internal Organs, American Society of Transplant Surgeons, American Association for Thoracic Surgery and Thoratec Inc. have supported the use of the Mechanical Circulatory Support Database operated by the International Society of Heart and Lung Transplantation.

8. Public Comments

CMS received one letter endorsing Medicare coverage signed by over 70 physicians. Other commenters suggested that Medicare restrict the centers that are allowed to perform this service to heart transplant centers that have experience with VADs as bridge to transplant, have nursing staff dedicated to VAD patients and have active biomedical engineering programs. Comments were also received suggesting that the DRG payment be increased to adequately reimburse hospitals for their costs.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is to be covered nationally under title XVIII of the Social Security Act § 1869(f)(1)(B). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, the expenses incurred for items or services must be “reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.” § 1862(a)(1)(A).

Question 1: Is the quality of the evidence adequate to draw conclusions about the impact of LVAD implantation on net health outcomes in Medicare beneficiaries meeting the Randomized Evaluation of Mechanical Assistance for the Treatment of Heart Failure (REMATCH) trial criteria who undergo LVAD implantation?

REMATCH demonstrated that even in a preponderantly elderly population with contraindications to cardiac transplantation, with careful patient selection, appropriate surgical management, and long term support of both the patient and family, an LVAD can increase length of life and improve its quality with prolonged periods of time outside the hospital.

REMATCH was a carefully constructed, randomized, multi-site clinical trial, whose participants were well matched in terms of such base-line characteristics as age, LVEF, NYHA class and medications. The number of participants was relatively small and included few women (about 20%), but results showed a statistically significant mortality advantage for patients receiving an LVAD and improved quality of life and functional status at one and two years. Additional experience with use of LVADs has demonstrated that they can sustain life for as long as several years (with interim device replacement if necessary) when used as a bridge to recovery or transplantation, with patients surviving for long periods outside of the hospital and in some cases recovering sufficient cardiac function to have the device removed. Even in REMATCH, two patients receiving devices recovered sufficiently to become transplant candidates although transplantation proved successful in only one.

The main questions not completely resolved on the basis of this evidence are:

- Would the same results be obtained in a larger group of patients or those with somewhat different selection criteria?
- Were there unique circumstances such as expertise available in a particular facility or an unusual combination of conditions in particular patients (even their gender) that affected their outcomes?
- Did modifications made to the device after the start of the study impact results either positively or negatively?
- What will be the average time to device failure when the device is made available to larger numbers of patients outside of a formal study environment?
- Do the results adequately reflect the full range of outcomes (both positive and negative) that might be expected from more wide spread use?
- Some inferences can be drawn from the bridge experience, but will they hold true in additional destination patients?

Even with these questions not fully resolved, REMATCH must be viewed as a successful trial. However, before coverage can be extended widely, CMS believes additional data will need to become available to provide assurance that the unanswered questions will not negatively impact future outcomes of this therapy for Medicare beneficiaries.

It must also be remembered that LVADs implanted as destination therapy are very expensive with average hospital charges running in excess of $200,000. Complications such as bleeding and infections led to additional hospital confinements as did device failures, which necessitated additional surgery for replacement of all or part of the device.

In summary, CMS believes that REMATCH provides adequate evidence that LVADs as destination therapy can provide positive net health outcomes in carefully selected patients and intends to provide coverage for that patient population. CMS also recognizes that the available evidence has important limitations, and additional studies are needed to more fully and reliably document risks and benefits of this evolving technology.

2. Do the results of the literature review indicate that CMS should require specific facility and personnel requirements that must be met to provide the patient with an optimal chance of successful LVAD implantation?

CMS has significant concerns as to whether the results obtained in clinical trials of new and high-risk procedures can be matched in all Medicare-approved facilities. Responsible translation and dissemination of new technology is critical to ensuring that Medicare beneficiaries have the best chance for optimal results. In a recent decision on lung volume reduction surgery (LVRS),

(http://www.cms.gov/mcd/viewdecisionmemo.asp?id=39), CMS determined that LVRS would be reasonable and necessary only when performed in facilities that had been identified by the National Heart, Lung, and Blood Institute (NHLBI) as meeting the thresholds for participation in the National Emphysema Treatment Trial (NETT) and at sites that have been approved by Medicare as lung transplant facilities. CMS felt that this new, difficult procedure, with a high mortality would be best performed at these centers of excellence until such time as an accreditation process could be developed. We have some of the same concerns about LVAD implantation as destination therapy.

Investigators participating in the REMATCH trial suggested both professional and facility criteria that they felt were important to the success of destination therapy:

Professional Criteria:

Cardiologist –

- Experienced and trained in management and treatment of end-stage heart failure
- Understanding of advanced heart failure therapies and experience with VADs.

Cardiac Surgeon –

- Experience in evaluating therapeutic options for patients with heart failure
- Previous experience and recently trained in VAD implantation

Facility Criteria:

- Experienced team trained and equipped to manage patients with end-stage heart failure and VADs
- Experience with open heart surgery and dedicated cardiac care unit
- Diagnostic and support services for full evaluation and follow up including: cardiology; anesthesiology; immunology; infectious disease; pulmonology; nephrology; social services; patient education; psychological support including end-of-life; nutrition; radiology and nursing

All facilities participating in REMATCH were already approved by Medicare to perform cardiac transplantation and had prior experience with LVAD implantation as a bridge to transplantation for patients on their transplant lists. CMS believes that the professional staff, infrastructure and support system available at many transplant facilities are crucial to the successful implementation of a destination therapy program. The existence of these factors will increase the likelihood of both appropriate assessment of the patient's lack of suitability for transplantation, and successful implantation of the destination therapy device. Also, transplant centers are more likely to have the necessary patient support systems in place to monitor the crucial post-operative and post-hospitalization periods.

However, unlike with NETT, CMS is not comfortable that using participation in the REMATCH trial should be the determinant for coverage of destination therapy beyond the trial setting. In NETT there was a formal application process for participation with a review and selection process managed by NIH, which did not exist for REMATCH. In fact, several proposed REMATCH facilities changed before the trial began and some selected facilities did not participate. Also, following conclusion of the trial some facilities have not continued to implant devices. Therefore, we cannot assume that all facilities that were a part of REMATCH should automatically be approved for reimbursement for destination therapy. The recent volume of LVAD implantations for either bridge-to-transplant or destination therapy is a more accurate predictor of the facility's ability to successfully perform this procedure. Facilities that routinely and repeatedly perform this surgery and follow patients for long periods of aftercare have a greater chance of successful outcomes. The volume necessary to achieve this goal is not presently known. Therefore, until center selection criteria are developed, CMS is establishing an interim minimum volume of 15 LVAD implantations, performed between January I, 2001 and September 30, 2003, as a prerequisite to Medicare reimbursement. In addition to this volume requirement, the LVADs must have been implanted either as a bridge to transplant or as destination therapy and must have been FDA-approved for one of these two indications or have been implanted as part of an FDA IDE trial for one of these two indications. LVADs implanted for support of blood circulation post cardiotomy or other investigational indications do not satisfy the volume requirement for this purpose. Since the relationship between volume and outcomes has not been well-established for LVAD use, facilities that have minimal deficiencies in meeting this standard may apply to the CMS Administrator for an exception based upon additional factors. Some of the factors that we will consider are geographic location of the center, number of destination procedures done and patient outcomes from LVAD procedures completed.

CMS will solicit input as to the appropriate mechanism for developing and implementing center selection criteria in the future. These criteria will be necessary prior to expanding beyond the initially approved sites and those granted an exception.

One element of determining whether a service is reasonable and necessary and thus covered by Medicare is whether a reasonable person, adequately informed of the risks and benefits, would choose to receive the service. In the case of LVADs, the risks of the procedures are such that patient education prior to the procedure is crucial. The informed consent process must be truly informed with guidance provided by competent individuals with the knowledge and time to give extensive, detailed, objective information to the beneficiary.

The patient’s decision to receive an LVAD is life altering both for himself and his family or companion, including consideration of the need for having assistance available in the home 24 hours per day. Recipients must learn to properly maintain the device, to use the emergency power pack, and to recognize operating problems. Additionally, the patient needs to avoid several hazards or sources of damage including tight clothing, water, and static electricity. Important characteristics of the patient’s home needs to be adequately assessed, including electrical wiring, and location of and accessibility of bedroom and shower. Considerations for traveling include avoiding potential injury by a deploying airbag, proximity to airport X-Ray machines and to carrying needed supporting equipment.

CMS expects that each institution will develop an informed consent document that would be understandable to all potential LVAD recipients. Such a document should be understandable by people at all educational levels and appropriate to the potential recipient’s level of education. Apart from the need to employ specifically defined medical terms, the document should in most circumstances be written for readers with no higher than an 8th or 9th grade level of education. If the potential recipient does not speak English, there should be an independent interpreter to facilitate understanding in the patient’s language. Where appropriate, translations of such a document and accompanying materials should be made available. Additional material explaining day-to-day operating requirements for living with an LVAD also should be made available to the patient by the device manufacturer prior to implantation.

CMS further expects that the following elements be incorporated in the informed consent document given to the potential LVAD recipient, with specific descriptions that would ensure the patient's awareness of:

1. The evaluation process.
2. The surgical procedure.
3. Alternative treatments.
4. Potential medical risks such as infection and bleeding with national and center-specific rates.
5. Device reliability/longevity.
6. National and facility-specific short-term and long-term mortality.
7. National and facility-specific outcomes other than mortality.
8. National and facility-specific lengths of stay.
9. Logistical support required at the patient’s home post-surgery.
10. Potential risk factors that could affect the immediate or future success of the surgery or the health of the patient, such as the patient’s history and the potential for device failure
11. His or her right to have the device turned off or to not be replaced, if malfunctioning.
12. His or her right to refuse the surgery.

CMS recognizes that institutions operating in different states may have different laws and needs that will affect the precise wording of the informed consent document(s) they will use. For that reason, these consent documents must be tailored to the specific needs and regulations under which each facility operates.

Moreover, CMS does not believe that forms are a substitute for in-person communication between physicians and other involved professionals and the potential recipient and his family. These forms should be viewed instead only as the written evidence of discussions leading to informed consent based upon full disclosure. Due to the significant time commitment required for full disclosure, CMS expects that each facility will train and assign to each potential destination therapy patient an advocate who would assist the operating team and facility supporting staff in insuring that full disclosure occurs. This individual should not be directly affiliated with the hospital surgical department or medical team that will perform the LVAD implantation and care for the recipient.

3. Does the limited data available indicate that CMS should require ongoing data collection for all LVAD implantations in Medicare beneficiaries to further refine appropriate patient and facility selection?

There are no other reported, completed, controlled studies of LVADs for destination therapy besides REMATCH. It would be preferable for additional patients implanted in the future to be part of randomized control trials that permit accrual of additional data about the longer term outcomes to be expected with LVAD use. That would ensure the most reliable information for future decisions. However, we recognize that such trials are unlikely for this technology.

The International Society of Heart and Lung Transplantation has expressed concerns about the inappropriate proliferation of destination therapy and the potential for harm to the patient if the medical and surgical personnel and the institutional team lack the expertise necessary to maximize the potential for survival advantage. They also expressed concern that inappropriate selection of patients for implantation, who could have been successfully managed medically, might diminish or eliminate the survival advantage seen in REMATCH. They, therefore, strongly support collection of additional data through a registry.

The LVAD is a complex device requiring a technically demanding surgical procedure for proper implantation. The procedure, the device and post-operative care will continue to be refined in coming years and it is important to have a means of assessing the quality of patient care over time to ensure that outcomes are maintained or ideally improved. Registry data will permit facilities to compare their LVAD experience against that of other implanting facilities to determine the quality of their performance overall as well as to assess whether an individual patient's care and progress in recovering from the procedure is meeting normative standards. For example, is the patient developing unusual complications or failing to respond as expected to usual care, possibly indicating the existence of patient specific problems such as lingering untreated infection or malnourishment that has not been effectively addressed? Are patients in a particular facility experiencing a higher than expected number of bleeding episodes, which could indicate problems with the a particular surgical team or are there an unusual number of device problems, battery failures, etc, which might indicate problems with the device or with a patient's training or understanding of necessary maintenance procedures?

Registry data can be an invaluable aid to an implanting facility in ongoing assessment of the quality of care it is providing to its patients. As part of its approval of destination therapy, the FDA is requiring that data for the 100 implantations following approval be reported through a registry. We agree with the FDA that data on more than the initial 68 REMATCH patients is needed to support and possibly expand this therapy. Because the length of survival to be expected for destination therapy is still unknown, CMS believes that long term outcomes data on all recipients is needed to provide patients with the information that they need in making an informed choice about whether to have this surgery.

Thus, CMS concludes that collection of data by a registry is crucial to provide access to information necessary to support advancement of this technology. This registry should include data from all LVAD recipients from the time of implantation through the remainder of their lives. Such a registry should be national in scope, developed and managed by a reputable organization, and be routinely audited.

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1 www.sf-36.com

2 www.mlhfq.org

3 http://www.clevelandclinic.org/quality/08-04/08-04b.htm

4 http://www.hcoa.org/hcoacme/chf-cme/chf00070.htm

5 Letter from Marvin A. Konstam, President, Heart Failure Society of America. June 19, 2003

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